



Synthesis, structural and vibrational properties of 1-(4-Fluorobenzoyl)-3-(isomeric fluorophenyl)thioureas

Aamer Saeed^{a,*}, Mauricio F. Erben^b, Uzma Shaheen^a, Ulrich Flörke^c

^a Department of Chemistry, Quaid-I-Azam University, Islamabad 45320, Pakistan

^b CEQUINOR (UNLP, CONICET-CCT La Plata), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, C.C. 962 (1900) La Plata, República Argentina, Argentina

^c Department Chemie, Fakultät für Naturwissenschaften, Universität Paderborn, Warburgerstrasse 100, D-33098 Paderborn, Germany

ARTICLE INFO

Article history:

Received 25 March 2011

Received in revised form 6 May 2011

Accepted 26 May 2011

Available online 13 June 2011

Keywords:

1-(4-Fluorobenzoyl)-3-(isomeric fluorophenyl)thioureas

Crystal structure

Conformer

Hydrogen bonds

Quantum chemical calculations

Vibrational studies

ABSTRACT

The 1-(4-Fluorobenzoyl)-3-(isomeric fluorophenyl)thioureas (**1–3**) were prepared by the reaction of 4-fluorobenzoyl isothiocyanate produced *in situ* with isomeric fluoroanilines in dry acetonitrile in good yields. The novel compounds were characterized by multinuclear (¹H and ¹³C) NMR, elemental analyses and FTIR spectroscopy techniques. Structural and conformational properties of compounds **1–3** have been analyzed using a combined approach including X-ray diffraction, vibrational spectra and theoretical calculation methods. The carbonyl and thiourea groups are almost planar and the conformation adopted by the C=S and the C=O double bonds is antiperiplanar, in a conformation which is stabilized by intramolecular N–H···O hydrogen bond. Crystal packing shows molecules connected by intermolecular N–H···S=C hydrogen bonds to form centrosymmetric dimers.

© 2011 Elsevier B.V. All rights reserved.

1. Introduction

1-Aroyl-3-arylthioureas found a wide diversity of applications in heterocyclic syntheses, metal complexes and molecular electronics and exhibit an array of biological activities [1–4]. Thus, besides the academic interest, *N,N*-dialkyl-*N'*-aroyl thioureas are efficient ligands for the separation of platinum group metals [5]. Thiourea complexes are starting materials in chemical spray pyrolysis (CSP) processes which are used to produce thin films of binary and ternary sulfides [6]. Fluorinated aryl thioureas represent a new class of potent anti-trypanosomal agents [7] and also a novel class of potent influenza virus neuraminidase inhibitors [8]. 1,3-Dialkyl or diaryl thioureas exhibit significant antifungal activity against plant pathogens *Pyricularia oryzae* and *Drechslera oryzae* [9]. *N*-Aryl *N*-phenyl thioureas have been developed as anion-binding site in a hydrogen-bonding receptor [10]. Thiocalix [4] arenes containing thioureas are neutral receptors towards α,α -dicarboxylate anions [11] and *N*-4-substituted-benzyl-*N'*-*ter*-butylbenzyl thioureas are vanilloid receptors ligands and antagonists in rat DRG neurons [12]. 1-Benzoyl-3-(4,6-disubstituted-pyrimidinyl) thioureas have shown excellent herbicidal activity [13]. Thioureas have also extensively been used in enantioselective synthesis, such as

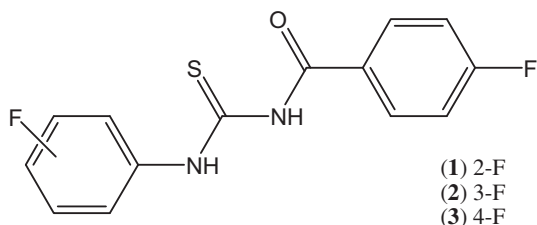
nitro-Mannich reactions, Aza-Henry reaction, and the Michael Addition [14–16]. In particular, fluorinated thioureas are convenient synthons for preparation of versatile fluorine-containing heterocycles: [1,3]-benzothiazin-4-ones [17], 1-aryl-2-ethylthioquinazolin-4-one, thiazolidine and 1*H*-1,2,4-triazoles [18].

Fabbrizzi et al. reported that substituted-phenyl urea compounds interacts through hydrogen bonding with a variety of oxoanions to give bright colored complexes [19]. A variety of receptors containing the urea and the thiourea groups have been designed for anion recognition [20]. In this context, the molecular structure and conformational flexibility are important properties for determining the donor–acceptor capabilities [21,22]. Also the thioureas can denature proteins, and inhibit the formation of micelles. Therefore the conformational issues in thioureas are comparable to those arising in folded proteins, and a complete understanding of these effects require understanding the effects of intermolecular hydrogen bonding interactions and hydrophobic interactions [20].

In view of the above mentioned facts and in continuation of our work on the synthesis and structural studies of thioureas, here we report the preparation, characterization and structural determination of three novel 1-(4-fluorobenzoyl)-3-(isomeric fluorophenyl)thiourea derivatives (**1–3**). Vibrational and conformational properties are studied by using quantum chemical calculations and vibrational spectroscopy techniques.

* Corresponding author. Tel.: +92 51 9064 2128; fax: +92 51 9064 2241.

E-mail address: aamersaeed@yahoo.com (A. Saeed).



Scheme 1.

2. Results and discussion

2.1. Synthesis and characterization

The title 1-(4-fluorobenzoyl)-3-(isomeric fluorophenyl)thioureas were prepared using a method similar to that reported earlier for related 1-(2-chlorobenzoyl)-3-(isomeric fluorophenyl)thiourea isomers [23] in 60–84% yields (Scheme 1). Table 1 gives the elemental, mass spectrometry and NMR spectroscopic data of compounds (1–3).

2.2. X-ray molecular structure

The molecular structures of compounds 1–3 as determined in the crystalline phase are shown in Figs. 1–3, respectively and Table 2 includes selected geometric parameters derived from the structure refinement, as well as those obtained from quantum chemical calculations.

The three molecular structures differ from the fluoro-substitution pattern of the thiobenzamide ring. Minor differences have been observed in the molecular geometry determined for the three isomers when the crystal structure is compared. For example, the two aromatic planes form dihedral angles each of 38.20(4)°, 8.20(12)° and 43.81(9)° for 1–3, respectively. The carbonyl and thiourea groups O1/C8/N2/C7/S1/N1 are almost planar, largest deviations from mean planes are 0.074(1), 0.053(2), and 0.019(3) Å for 1, 2, and 3, respectively. Associated are intramolecular N1–H···O1 hydrogen bonds forming six-membered rings for all three structures. Dihedral angles between these carbonyl thiourea planes and the fluorophenyl/*p*-fluorophenyl rings measure for 1: 21.35(5)°/18.51(6)°, for 2: 14.44(11)°/22.57(10)°, for 3: 52.32(7)°/9.24(13)°.

It was observed that the amidic N2–C8 [1.377(2) Å] and thioamide N1–C7 [1.401(2) Å] bond lengths (mean values are given)

are shorter than C–N single bond [24], indicating a partial double bond character. This observation indicates that resonance interactions are extended over the whole planar –C(O)NHC(S)NH– moiety, in accordance with the behavior recently reported for thiocarbamate species [25]. Moreover, it is worth noting that a definite trend in the C–N bond distances has been recognized for these species [5,26], the lengths increasing in the order C7–N1 < C8–N2 < C7–N2. This tendency is also reproduced by the quantum chemical calculations (see Table 1), suggesting that intramolecular electronic effects are responsible for the observed N–C bond lengths values. The different fluoro substitution has no significant effect on N1–C1 or N1–C7 bond length parameters.

Crystal packing shows for 1–3 intermolecular N1–H···S hydrogen bonds, forming centrosymmetric dimers, as shown in Figs. 4–6, with N–H···S contacts of 2.594, 2.908 and 2.781 Å, respectively. This is a well-known crystal motif for *N*-benzoyl-thiourea compounds [25–27], for which the character of the *N*-substituents seems to exert little impact. Intermolecular N1···S short distances amount 3.374(1), 3.722(2) and 3.631(3) Å for compound 1–3, respectively. The shortest intermolecular C–H···F distances are in the 2.46–2.82 Å range, a short intramolecular N2–H···F distance in 2 measures 2.50 Å.

2.3. Conformational analysis

In principle, the studied compounds may adopt several conformations depending on the relative orientation of the C=O and C=S double bonds and the orientation of substituted phenyl rings. However, several authors [26,27] pointed out that the conformational properties of substituted benzoyl thioureas is mainly dominated by the conformational behavior around the C–N bond joining the amide and thioamide groups. This is also in agreement with our recent work on the conformational space of isomeric 1-(2-chlorobenzoyl)-3-(isomeric fluorophenyl)thiourea derivatives [28]. Based on the X-ray structural results, the substituted phenyl rings were maintained in a conformation close to the experimental X-ray crystal structure, while the potential energy curve around the C7–N2 bond for compounds 1–3 have been theoretically evaluated. Thus, the potential energy curves were computed at the B3LYP level of approximation together with the split-valence triple-zeta basis set 6-311G*, allowing geometry optimizations with the δ (C8N2–C7N1) dihedral angle varying from 0° to 360° in steps of 20°. These curves are displayed in Fig. 7. The three potential energy curves are very similar, showing a clear minimum at δ (C8N2–C7N1) = 0°, corresponding to a local planar structure of the central –C=O–NH–C=S–NH– moiety, with opposite orienta-

Table 1
Elemental mass and NMR spectroscopic data for compounds 1–3.

Comp.	Molecular formula (MW)	EIMS (M ⁺)	Analysis (Calcd./Found)				¹ H NMR δ (ppm), J (Hz)	¹³ C NMR δ (ppm) J (Hz)
			C (%)	H (%)	N (%)	S (%)		
1	C ₁₄ H ₁₀ N ₂ OSF ₂ (292.3)	292.0	57.53/	3.45/	9.58/	10.97/	12.43 (<i>br s</i> , 1H, NH), 9.65 (<i>br s</i> , 1H, NH), 8.45 (<i>dt</i> , J = 2.1, 7.5 Hz, 1H, Ar–H), 8.07–7.05 (<i>m</i> , 7H, Ar–H)	177.5 (C=S), 166.8 (C=O), 164.9 (<i>d</i> , ¹ J = 250 Hz), 155.0 (<i>d</i> , ¹ J = 247 Hz), 133.0 (2C, ³ J = 8.25 Hz), 131.6, 127.8 (<i>d</i> , ³ J = 8.25 Hz), 125.9 (<i>d</i> , ³ J = 10.5 Hz), 125.2, 124.1 (<i>d</i> , ⁴ J = 3.75 Hz), 115.6 (<i>d</i> , ² J = 19.5 Hz), 114.8 (2C, ² J = 21.75 Hz)
			57.59	3.42	9.62	11.01		
2	C ₁₄ H ₁₀ N ₂ OSF ₂ (292.3)	292.0	57.53/	3.45/	9.58/	10.97/	12.39 (<i>br s</i> , 1H, NH), 9.69 (<i>br s</i> , 1H, NH), 8.08–8.00 (2H, <i>m</i> , Ar–H), 7.77 (<i>td</i> , J = 2.1, 10.2 Hz, 1H, Ar–H), 7.43–6.96 (<i>m</i> , 5H, Ar–H)	178.0 (C=S), 166.6 (C=O), 165.5 (<i>d</i> , ¹ J = 244.5 Hz), 164.9 (<i>d</i> , ¹ J = 250 Hz), 138.9 (<i>d</i> , ³ J = 10.5 Hz), 133.0 (2C, ³ J = 8.25 Hz), 131.6, 130.6 (<i>d</i> , ³ J = 9.75 Hz), 119.4 (<i>d</i> , ⁴ J = 3 Hz), 114.8 (2C, ² J = 21.25 Hz), 113.8 (<i>d</i> , ² J = 21.75 Hz), 114.8 (2C, ² J = 21.75 Hz)
			57.47	3.40	9.62	10.93		
3	C ₁₄ H ₁₀ N ₂ OSF ₂ (292.3)	292.0	57.53/	3.45/	9.58/	10.97/	12.7 (<i>br s</i> , 1H, NH), 9.16 (<i>br s</i> , 1H, NH), 8.07–6.95 (<i>m</i> , 8H, Ar–H)	178.2 (C=S), 166.4 (C=O), 164.9 (<i>d</i> , ¹ J = 250 Hz), 161.0 (<i>d</i> , ¹ J = 246 Hz), 133.6 (<i>d</i> , ⁴ J = 3 Hz), 133.0 (2C, ³ J = 8.25 Hz), 131.7, 126.3 (2C, ³ J = 8.25 Hz), 115.8 (2C, ² J = 22.5 Hz), 114.9 (2C, ² J = 21.7 Hz)
			57.59	3.39	9.48	10.90		

Download English Version:

<https://daneshyari.com/en/article/1409377>

Download Persian Version:

<https://daneshyari.com/article/1409377>

[Daneshyari.com](https://daneshyari.com)